

CLAIMS:

1. A method for determining predisposition to a physiological reaction of an individual to a biologically active compound comprising characterizing nucleotide sequence of at least one of the *UGT1A1*, *UGT1A7* or *UGT1A9* gene or a part thereof of said individual, wherein the presence of at least one polymorphic or haplotypic variation in said nucleotide sequence is indicative of said predisposition to a physiological reaction.
2. The method of claim 1, wherein said predisposition is a hereditary predisposition.
3. The method of claim 1, wherein said predisposition is a higher or lower susceptibility, sensibility, diathesis, proneness, proclivity, tendency, sensitivity, responsiveness, resistance or constitutional sickness to said physiological reaction.
4. The method of claim 1, wherein said physiological reaction is a beneficial reaction.
5. The method of claim 1, wherein said physiological reaction is an adverse reaction or a side effect.
6. The method of claim 1, wherein said biologically active compound is a xenobiotic.
7. The method of claim 6, wherein said xenobiotic is a drug, a carcinogen or a pre-carcinogen.
8. The method of claim 7, wherein said drug is an anti-cancer agent or an immunosuppressive agent.
9. The method of claim 8, wherein said anti-cancer agent is a camptothecin or an analog thereof.

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10. The method of claim 9, wherein said camptothecin analog is 7-ethyl-10-[4-(1-piperidino)-1-piperidino] carbonyloxy camptothecin (irinotecan, CPT-11), 7-ethyl-10-hydroxycamptothecin (SN-38).
11. The method of claim 8, wherein said immunosuppressive agent is mycophenolic acid (MPA).
12. The method of claim 1, wherein said individual is a human or an animal.
13. The method of claim 1, wherein said individual is a patient with cancer.
14. The method of claim 13, wherein said patient has a colorectal cancer or a solid tumor.
15. The method of claim 1, wherein determining genetic sequence is performed on a DNA or a RNA sample.
16. The method of claim 1, wherein said polymorphic or haplotypic variation is a UGT1A9 variation.
17. The method of claim 16, wherein said UGT1A9 variation is at least one of a C⁻²²⁰⁸T substitution, a C⁻²¹⁵²T substitution, a C⁻²¹⁴¹T substitution, a T¹⁸⁸⁷G substitution, a T¹⁸¹⁸C substitution, a C⁻⁶⁶⁵T substitution, a T⁻⁴⁴⁰C substitution, a C⁻³³¹T substitution, a T²⁷⁵A substitution, a G⁻⁸⁷A substitution, a G⁸A missence mutation (C³Y), a T⁹⁸C missence mutation (M³³T) or combination thereof.
18. The method of claim 17; wherein said G⁸A missence mutation is associated with a decreased predisposition or susceptibility to an anti-cancer agent.
19. The method of claim 17, wherein said G⁸A missence mutation is associated with a decreased responsiveness to an immunosuppressive agent.

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20. The method of claim 17, wherein said T⁹⁸C missense mutation is associated with an increased adverse reaction to an anti-cancer agent.

21. The method of claim 1, wherein said polymorphic or haplotypic variation is a UGT1A7 variation.

22. The method of claim 21, wherein said UGT1A7 variation is a G³⁵³T missense mutation, a T³⁹⁷G missense mutation, a C⁴⁰¹A missense mutation, a G⁴⁰²A missense mutations, a G⁴²⁷C missense mutation, a T⁶³²C missense mutation or combination thereof.

23. The method of claim 1, wherein said polymorphic or haplotypic variation is a UGT1A1 variation.

24. The method of claim 23, wherein said UGT1A1 variation is a TA₇ mutation in the TATA box.

25. An isolated nucleotide sequence comprising at least one nucleotide sequence selected from the group consisting of SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, a fragment or the complementary sequences thereof, for determining predisposition to a physiological reaction.

26. The nucleotide sequence of claim 25, wherein said sequence is an allelic variant of UGT1A1, UGT1A7 or UGT1A9.

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27. An isolated amino acid sequence comprising at least one amino acid sequence selected from the group consisting of SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71 or a fragment thereof.
28. The amino acid sequence of claim 27, wherein said sequence is encoded by a nucleotide sequence comprising at least one sequence selected from the group consisting of SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, a fragment or the complementary sequences thereof.
29. The amino acid sequence of claim 27, wherein the expression of said sequence is regulated by a nucleotide sequence comprising at least one sequence selected from the group consisting of SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, a fragment or the complementary sequences thereof.